(FILE 'HOME' ENTERED AT 16:42:17 ON 01 APR 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 16:42:25 ON 01 APR 2003

L1 407 S (TUMOR INVASION) (L) INTEGRIN
L2 181 DUP REM L1 (226 DUPLICATES REMOVED)
L3 112 S L2 AND ALPHA?
L4 112 FOCUS L3 1-
L5 62 S L4 AND PY<=1998
L6 62 FOCUS L5 1-
L7 17 S L6 AND (INTEGRIN (L) BINDING)
L8 17 FOCUS L7 1-

=> d an ti so au ab pi 16 8

L6 ANSWER 8 OF 62 CAPLUS COPYRIGHT 2003 ACS
AN 1992:171290 CAPLUS
DN 116:171290
TI Role of the .**alpha**.v.beta.3 integrin in human melanoma cell invasion
SO Proceedings of the National Academy of Sciences of the United States of America (**1992**), 89(5), 1557-61
CODEN: PNASA6; ISSN: 0027-8424
AU Seftor, Richard E. B.; Seftor, Elisabeth A.; Gehlsen, Kurt R.; Stetler-Stevenson, William G.; Brown, Peter D.; Ruoslahti, Erkki; Hendrix, Mary J. C.
AB The human melanoma cell line A375M expresses the vitronectin receptor (.**alpha**.v.beta.3 integrin) on its cell surface. Treatment of A375M cells with either polyclonal or monoclonal anti-.**alpha**.v.beta.3 antibodies resulted in stimulation of invasion through basement membrane matrixes in vitro. Similar treatment of these cells with a monoclonal anti-.**alpha**.v antibody, which does not inhibit the adhesive function of the .**alpha**.v.beta.3 antigen, also stimulated invasion; however, anti-.beta.3 antibody treatment had no effect. Furthermore, pretreatment of the cells with vitronectin or addn. of vitronectin to the basement membrane matrix also resulted in stimulation of invasion. Similar treatments with fibronectin receptor antibody or fibronectin had no effect on invasion. Anal. of type IV collagenase expression in cells treated with anti-.**alpha**.v.beta.3 antibody showed higher levels of both the secreted 72-kDa enzyme and its mRNA. Signal transduction through the .**alpha**.v.beta.3 integrin could underlie the elevated expression of metalloproteinase and the enhanced invasion of A375M cells through basement membrane matrixes.

L4 ANSWER 3 OF 112 MEDLINE

AN 97160578 MEDLINE

TI Ligation of integrin **alpha5beta1** is required for internalization of vitronectin by integrin **alphavbeta3**.

SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Jan 31) 272 (5) 2736-43. Journal code: 2985121R. ISSN: 0021-9258.

AU Pijuan-Thompson V; Gladson C L

AB Remodeling of the matrix by tumor cells is necessary for **tumor invasion**. We have shown previously that malignant astrocytomas, in contrast to normal astrocytes, synthesize vitronectin and express **integrins alphavbeta3** and **alphavbeta5**. The activity states of these two **integrins** are differentially controlled. Thus, we investigated the regulation of the activity of **integrins alphavbeta3** and **alphavbeta5** with regard to their role in vitronectin internalization in U-251MG astrocytoma cell monolayers adherent to fibronectin, collagen, or laminin in serum-free conditions. Binding of [125I]vitronectin occurred in a specific, saturable manner that was partially inhibitable by monoclonal antibodies (mAbs) specific for **integrins alphavbeta3** or **alphavbeta5**. Specific, lysosomally-mediated degradation of [125I]vitronectin was detectable at 1 h and increased over the 24-h assay period. The cell substrate affected the rate of turnover of [125I]vitronectin, which was 3.0 ng/min for cells plated on fibronectin but 0.35 ng/min for cells plated on collagen. Furthermore, although mAbs specific for either **integrin alphavbeta3** or **alphavbeta5** inhibited degradation (30%; combined effect 70%) of [125I]vitronectin by cells plated on fibronectin, only mAb anti-**alphavbeta5** inhibited degradation (70-90%) by cells plated on collagen or laminin. To determine the requirement for **integrin alpha5beta1** ligation in order for **integrin alphavbeta3** to internalize its ligand, cells were plated on mAbs anti-**integrin alpha5** or anti-**integrin alpha3**. When plated on mAb anti-**alpha5**, mAbs anti-**alphavbeta3** and anti-**alphavbeta5** both inhibited degradation. However, when plated on mAb anti-**alpha3**, mAb anti-**alphavbeta3** had no effect whereas mAb anti-**alphavbeta5** inhibited degradation. These data indicate that a signal from **integrin alpha5beta1** is necessary for **integrin alphavbeta3** to internalize vitronectin, whereas **integrin alphavbeta5** constitutively internalizes vitronectin.

ANSWER 8 OF 17 MEDLINE

AN 1998389907 MEDLINE

TI Growth factor-dependent activation of **alphavbeta3** **integrin** in normal epithelial cells: implications for **tumor invasion**.

SO JOURNAL OF CELL BIOLOGY, **(1998 Aug 24)** 142 (4) 1145-56. Journal code: 0375356. ISSN: 0021-9525.

AU Trusolino L; Serini G; Cecchini G; Besati C; Ambesi-Impiombato F S; Marchisio P C; De Filippi R

AB **Integrin** activation is a multifaceted phenomenon leading to increased affinity and avidity for matrix ligands. To investigate whether cytokines produced during stromal infiltration of carcinoma cells activate nonfunctional epithelial **integrins**, a cellular system of human thyroid clones derived from normal glands (HTU-5) and papillary carcinomas (HTU-34) was employed. In HTU-5 cells, **alphavbeta3** **integrin** was diffused all over the membrane, disconnected from the cytoskeleton, and unable to mediate adhesion. Conversely, in HTU-34 cells, **alphavbeta3** was clustered at focal contacts (FCs) and mediated firm attachment and spreading. **alphavbeta3** recruitment at FCs and ligand-**binding** activity, essentially identical to those of HTU-34, occurred in HTU-5 cells upon treatment with hepatocyte growth factor/scatter factor (HGF/SF). The HTU-34 clone secreted HGF/SF and its receptor was constitutively tyrosine phosphorylated suggesting an autocrine loop responsible for **alphavbeta3** activated state. Antibody-mediated inhibition of HGF/SF function in HTU-34 cells disrupted **alphavbeta3** enrichment at FCs and impaired adhesion. Accordingly, activation of **alphavbeta3** in normal cells was produced by HTU-34 conditioned medium on the basis of its content of HGF/SF. These results provide the first example of a growth factor-driven **integrin** activation mechanism in normal epithelial cells and uncover the importance of cytokine-based autocrine loops for the physiological control of **integrin** activation.

L6 ANSWER 13 OF 62 CAPLUS COPYRIGHT 2003 ACS
AN 1995:461347 CAPLUS
DN 122:211441
TI The .**alpha**.v integrins
SO Integrins Biol. Probl. (**1994**), 83-99. Editor(s): Takada, Yoshikazu. Publisher: CRC, Boca Raton, Fla.
CODEN: 60XYAR
AU Gladson, Candece L.; Cheresh, David A.
AB A review with 105 refs. Discussed are: structure of the .**alpha**.v **integrins**; ligand recognition; in vitro functions of .**alpha**.v **integrins**; cell and tissue expression; and examples of in situ functions (transformation and **tumor invasion**, development and differentiation, bone resorption, immune response).

L Number	Hits	Search Text	DB	Time stamp
-	18	(Receptor SAME (advanced ADJ glycation)) and RAGE	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2002/05/16 10:39
-	42	RAGE and (advanced ADJ glycation)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 14:15
-	34	(Receptor SAME (advanced ADJ glycation)) and (cancer or tumor or mata$10 or neoplas$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/28 15:25
-	77	Receptor SAME (advanced ADJ glycation)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 16:17
-	49	Receptor ADJ advanced ADJ glycation	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 14:47
-	5	(US-20020002203-$ or US-20010053357-$ or US-20010039256-$).did. or (WO-9918987-$).did. or (US-20010039256-$ or WO-200020458-$ or WO-200020621-$ or WO-9954485-$ or US-20010053357-$).did.	US-PGPUB; EPO; DERWENT	2003/03/27 14:45
-	4	(Receptor ADJ advanced ADJ glycation) SAME amphoterin	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 14:53
-	15	Morser ADJ Michael ADJ John	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 14:54
-	29	(US-6465422-$ or US-5864018-$ or US-5811401-$).did. or (US-20010039256-$ or US-20020002203-$ or US-20010053357-$ or US-20030059423-$ or US-20030037344-$ or US-20030032663-$ or US-20020177550-$ or US-20020122799-$ or US-20020116725-$ or US-20020106726-$ or US-20020013256-$ or US-20010041349-$).did. or (WO-9918987-$ or WO-9954485-$ or WO-9907402-$ or WO-9822138-$ or WO-9726913-$ or WO-9739121-$).did. or (WO-200020621-$ or WO-200020458-$ or WO-200274805-$ or WO-200230889-$ or US-20020116725-$ or US-20020106726-$ or US-6465422-$ or US-20010039256-$ or US-20010053357-$).did.	USPAT; US-PGPUB; EPO; DERWENT	2003/03/27 14:56
-	87	Receptor SAME advanced SAME glycation	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 16:18
-	0	(Receptor SAME advanced SAME glycation) and (extracelular SAME matri$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 16:19
-	26	(Receptor SAME advanced SAME glycation) and (laminin fibronectin amphoterin caderin integrin hyaluronic integrin amphoterin)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 16:26

-	104	RAGE and (laminin fibronectin amphoterin caderin integrin hyaluronic integrin amphoterin)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/27 16:26
-	99	(advanced ADJ glycation) and (cancer or tumor or mata$10 or neoplas$5)	USPAT; US-PGPUB; EPO; JPO; DERWENT; USOCR	2003/03/28 15:25
-	143	invasion SAME tumor SAME integrin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/01 15:32